Optical Mammography with Intensity-Modulated Light

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Abstract: We report the results of our initial analysis of the frequency-domain optical mammograms collected on a clinical population of 131 patients. The instrument for optical mammography employs four intensity-modulated (at 70 MHz) laser diodes emitting at 690, 750, 788, and 856 nm. The amplitude and phase images of the breast are combined to produce edge-corrected optical images at each of the four wavelengths. The one-wavelength (690 nm) edge-corrected images have been examined according to two different criteria for the assignment of positive optical mammograms. Criterion 1 requires both views of the breast to be positive, while criterion 2 requires at least one view to be positive. The resulting (sensitivity; specificity) was (72%; 52%) (criterion 1) and (88%; 30%) (criterion 2). We show how adding spectral information can improve on these results.

OCIS codes: (170.0170) Medical optics and biotechnology; (110.0110) Imaging systems; (170.4580) Optical diagnostics for medicine; (170.3830) Mammography; (110.7050) Turbid media

1. Introduction

Optical mammography is a safe, painless, and cost-effective technique that may become a useful clinical tool for the detection and diagnosis of breast cancer. It employs near-infrared light (typically in the wavelength range 670-970 nm) to non-invasively probe the female breast. Over this spectral region, hemoglobin is the dominant intrinsic contrast agent. The hemoglobin concentration and its oxygen saturation are two key parameters that may allow not only the detection of cancer, but also the discrimination between malignant and benign breast lesions using optical methods. Optical mammography can be performed using continuous wave (CW) light [1,2], or using time-resolved techniques in the time-domain [3-5] and in the frequency-domain [6-11]. Previous implementations of CW optical mammography in the 1970’s and 1980’s under the names of diaphanography [12] and lightscanning [13] failed to produce a viable clinical tool because of their inferior performance compared to x-ray mammography [14-18]. In the past decade, the use of diffusion theory to model light propagation into breast tissue, and the introduction of time-resolved optical methods have opened new possibilities in the area of optical mammography. Here, we present our approach to frequency-domain optical mammography, and we report the results of a preliminary analysis of the optical breast images collected on a clinical population of 131 patients.
2. Methods

The block diagram of the apparatus for frequency-domain optical mammography is shown in Fig. 1. This instrument is a four-wavelength, homodyne-in-quadrature system. The four wavelengths (690, 750, 788, 856 nm) are electronically discriminated by modulating the corresponding laser diodes at different frequencies ranging from 69.50 to 70.45 MHz. The modulation is achieved by superimposing a radio-frequency signal to the DC current supplies by means of bias tees. A modulation frequency in the order of 70 MHz is chosen to achieve a phase shift per unit distance of about $20^\circ$/cm in breast tissue. A pilot laser at 1310 nm, modulated at 500 kHz, is used to probe the geometrical shape of the breast and to drive protection switches that prevent the photomultiplier tube detector from being overexposed. The emission of the five laser diodes is guided by optical fibers (core diameter: 100 $\mu$m) to a fiber coupler. The output of the coupler is an optical fiber having an internal diameter of 400 $\mu$m. The numerical aperture of this fiber results in an illuminated area larger than 1 mm$^2$ on the breast surface. The maximum optical power emitted by the laser diodes at 690, 750, 788, 856, and 1310 nm is 30, 10, 40, 50, and 5 mW, respectively. About 70% of this optical power reaches the skin of the breast via the fiber optics. The maximum irradiance on the skin is therefore $0.7 \times 135$ mW/mm$^2$. This irradiance is kept on a given spot by no longer than the pixel residence time (8 ms) determined by the $x$-$y$ translational stage. Consequently, the maximum radiant exposure on the skin is $756$ mW-ms/mm$^2 = 75.6$ mJ/cm$^2$, which is significantly less than the maximum permissible exposure to a laser beam for skin (329 mJ/cm$^2$) reported by the American National Standard for the safe use of lasers under these conditions [19].

![Block diagram of the instrument for frequency-domain optical mammography. I: current; f: frequency; A: amplitude, $\phi$: phase; BT: bias tee; S: shutter; Discr.: discriminator; $x,y$ Trans.: $x,y$ translational stage; PMT: photomultiplier tube; ADC: analog to digital converter; MUX: multiplexer.](image)
The optical signal is collected in a transmission geometry by an optical fiber bundle having an internal diameter of 5 mm (core diameter of the individual fibers: 60 µm). The source and the detector fibers are located on opposite sides of the breast. About 90% of the collected optical signal is guided to a photomultiplier tube detector (for the 690, 750, 788, and 856 nm signals), and about 10% to a photodiode (for the 1310 nm pilot signal). The instrumental noise measured on a tissue-like phantom without x-y translational motion and with an acquisition time of 8 ms is 0.15% for the amplitude, and 0.1° for the phase. Mechanical scanning increases the instrumental noise. Typical noise levels recorded in a human breast examination (with translational motion, acquisition time per pixel: 8 ms, breast thickness: 4-8 cm) are 2-3% for the amplitude, and 0.5-0.8° for the phase.

During an examination, the breast is slightly compressed between two glass plates. The distance between the compressing plates is measured and recorded during each exam. The optical image of the breast is acquired by performing a continuous tandem scan of the source and detector fibers over the x-y plane defined by the compression plates. The source and detector fibers remain collinear while the scan is being performed. The resulting 2-dimensional projection image of the breast is made of $2 \times 2$ mm$^2$ pixels. The breast compression assembly can be rotated to allow the acquisition of breast images in the craniocaudal and oblique views, as routinely done also in x-ray mammography. The acquisition time required to image the whole breast is about 2 min per view.

The amplitude and phase data are combined into a dimensionless parameter, that we called $N$, which is related to the optical absorbance of breast tissue [20]. The images based on this parameter ($N$-images) accomplish a significant correction of edge effects, which are determined by the reduction in breast thickness and by the modified boundary conditions at pixels close to the edge of the breast [20]. As a result, the dynamic range of the $N$-images is significantly less than that of the amplitude and phase images, and optical inhomogeneities in the breast appear with a higher contrast. Furthermore, $N$-images are displayed using a linear gray scale over the full range of data in the image (white represents the lowest value, black the highest). This allows for the display of the optical images of the breast in real-time, on-line, during the examination. The examiner is not required to perform any further manipulations to the $N$-images after acquisition.

We have examined with frequency-domain optical mammography a clinical population of 131 patients. The diagnosis of the cases was determined either by fine needle biopsy or by pathology examination following surgery. In the interpretation of the optical mammograms, we have followed two distinct criteria. The first one (criterion 1), previously reported [21], considers an optical mammogram to be positive if it shows optical abnormalities that are spatially consistent in the two views and that are not thread like. The second one (criterion 2) requires an optical mammogram to show a suspicious region in at least one view to classify the case as a positive finding.

### 3. Results

The appearance of breast cancer in an optical mammogram is illustrated in Fig. 2. This figure reports the craniocaudal and oblique views, at 690 nm, of the left breast of a 72 year old patient affected by invasive ductal carcinoma. The cancer size is 2.5 cm. Despite the intrinsically low-resolution of optical mammography, the optical image shows this 2.5 cm-diameter cancer with high contrast. The optical contrast is mainly determined by an increased hemoglobin concentration around the cancerous tissue, which significantly increases the local absorption coefficient. The absorption coefficient of cancerous breast tissue can be 2-3 larger than the absorption coefficient of healthy breast tissue [22,23]. Because blood not only absorbs light, but it also scatters it, the smaller scattering contrast observed in breast cancers (factor 1-1.3) [22,23] may also result from the increased blood concentration in the cancerous area. We observe that the $N$-images are not able to discriminate absorption from scattering contrast.
The dark areas in the two images of Fig. 2 represent areas of higher optical absorbance, but they do not provide information on the relative absorption and scattering contributions to the increased absorbance. We have examined the one-wavelength (690 nm) N-images from the clinical population according to the two different criteria described in section 2. The results according to criteria 1 and 2 are reported in Table 1.

Fig. 2. Craniocaudal (cc) and oblique (ob) views of the left (L) breast of a 72 year old patient affected by invasive ductal carcinoma. Cancer size is 2.5 cm. The cancer appear with high contrast in both views of the breast.

Table 1. Results of the analysis of the 690 nm frequency-domain optical mammograms from a clinical population of 131 patients according to criteria 1 and 2.

<table>
<thead>
<tr>
<th></th>
<th>Both views requirement (Criterion 1)</th>
<th>At least one view requirement (Criterion 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive results (TP)</td>
<td>42</td>
<td>53</td>
</tr>
<tr>
<td>True negative results (TN)</td>
<td>79</td>
<td>52</td>
</tr>
<tr>
<td>False positive results (FP)</td>
<td>73</td>
<td>122</td>
</tr>
<tr>
<td>False negative results (FN)</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Sensitivity: TP/(TP+FN)</td>
<td>72%</td>
<td>88%</td>
</tr>
<tr>
<td>Specificity: TN/(TN+FP)</td>
<td>52%</td>
<td>30%</td>
</tr>
<tr>
<td>Pos. predictive value: TP/(TP+FP)</td>
<td>37%</td>
<td>30%</td>
</tr>
<tr>
<td>Neg. predictive value: TN/(TN+FN)</td>
<td>83%</td>
<td>88%</td>
</tr>
<tr>
<td>Test efficiency: (TP+TN)/Total results</td>
<td>58%</td>
<td>44%</td>
</tr>
</tbody>
</table>
The results of Table 1 are based on the $N$-images at one wavelength (690 nm). Additional information can be obtained by considering the images at the other three wavelengths (750, 788, and 856 nm). The specificity of the examination, and therefore the diagnosis potential, can benefit from the analysis of the spectral dependence of the detected breast lesions. For example, Fig. 3 reports the spectral dependences of three different optical inhomogeneities observed in three cases: (1) blood vessel, (2) cancer, and (3) mastopathy. The corresponding optical mammograms (at 690 nm, craniocaudal view) are illustrated on the right hand side of Fig. 3. In Fig. 3, one can observe that spectral features provide a discriminating capability that adds to the morphological information provided by single-wavelength $N$-images.

![Graph showing spectral discrimination of three structures (blood vessel, cancer, mastopathy)](image)

**Fig. 3.** Spectral discrimination of three structures (a blood vessel, a malignant tumor, and a mastopathy) observed in three optical mammograms.

### 4. Discussion and Conclusion

The results reported in Table 1 must be interpreted by considering that they are obtained from the analysis of one-wavelength $N$-images, which do not take full advantage of the potential of frequency-domain optical mammography. The characterization of the tumor optical properties, possibly by reconstructing the absorption and scattering images of the breast [9], and the analysis of spectral features, which may give indications on the oxygenation of breast lesions [8], are key factors in optical mammography. By fully exploiting these unique features, it may be possible to improve the performance of optical mammography to a level that renders it a clinically attractive technique.

### Acknowledgments

This work is sponsored by the Department of the Army, Award No. DAMD17-99-1-9218. The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the awarding and administering acquisition office. The material presented does not necessarily reflect the position or the policy of the Government, and no official endorsement should be inferred.
References


